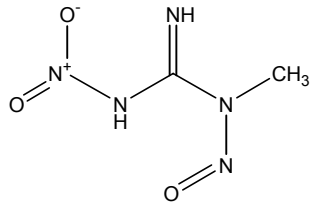
N-METHYL-*N*′-NITRO-*N*-NITROSOGUANIDINE
CAS No. 70-25-7

First Listed in the *Sixth Annual Report on Carcinogens*



CARCINOGENICITY

N-Methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity of in experimental animals (IARC V.4, 1974; IARC S.7, 1987). *N*-Methyl-*N*′-nitro-*N*-nitrosoguanidine is carcinogenic in all species tested: mouse, rat, hamster, rabbit, and dog. When administered in the drinking water of rats, MNNG induced adenomas, adenocarcinomas, a few leiomyosarcomas, and signet-ring cell carcinomas of the glandular stomach in rats. Additional malignant tumors were observed, especially at high concentrations, in the duodenum, jejunum and mesentery, together with papillomas in the forestomach and liver tumors. When administered in the drinking water, MNNG induced leiomyosarcomas in the walls of gastric cysts, neonatally grafted into the subcutaneous tissues of mice. When administered in the drinking water, MNNG induced adenocarcinomas and sarcomas of the glandular stomach of male hamsters. When administered in the drinking water, it induced adenocarcinomas in the stomach of the four dogs that were studied. Tumors were localized mainly in the cardiac portion and in the antrum. When administered by gavage, a single dose of MNNG induced three squamous cell carcinomas and one papilloma of the stomach in three of six male mice; the spontaneous occurrence of gastrointestinal tumors is considered extremely rare in the species used in this study. When administered by gavage as a single high dose, the compound induced malignant tumors in the glandular and forestomach of rats. When administered as a series of gavage treatments at irregular intervals, the compound induced squamous papillomas and squamous cell carcinomas of the forestomach and tumors in the glandular stomach, liver, and peritoneum in rats of both sexes. When administered by subcutaneous injection, the compound induced fibrosarcomas and polymorphic sarcomas at the injection site in adult rats. In a similar study, fibrosarcomas and rhabdomyosarcomas were induced at the injection site in male rats. Newborn rats that received a single subcutaneous injection of MNNG developed adenocarcinomas, fibrosarcomas, and myosarcomas of the small intestine. A single subcutaneous injection of MNNG induced lung and liver tumors and hemangioendotheliomas in mice. When administered by intraperitoneal injection, MNNG induced four benign and malignant tumors of the cecum, ileum, and jejunum in male mice. When administered by a single intraperitoneal injection, the compound induced tumors of the stomach, jejunum, and cecum in male rats and carcinomas and sarcomas of the stomach and small intestine in suckling rats. When administered by intrarectal instillation, the compound induced one or more adenomatous polyps and polypoid carcinomas in the colon and rectum of seven of nine rats. In recent studies not reviewed by an IARC Working Group, when administered topically, MNNG induced skin papillomas and carcinomas in male and female mice (O'Connell et al., 1987; Mitchell et al., 1988).

There is inadequate evidence for the carcinogenicity of *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine in humans. Three cases of brain tumor (gliomas) and one of colon cancer have been reported for workers in a genetics laboratory over a 13-year period. All the subjects had

probably been exposed to the compound for 6-15 years prior to death, but other carcinogens had been used in the laboratory (IARC V.4, 1974; IARC S.7, 1987).

PROPERTIES

N-Methyl-*N*′-nitro-*N*-nitrosoguanidine occurs as a pale yellow-to-pink crystalline powder that may become green or orange when exposed to light. MNNG is soluble in polar organic solvents but decomposes in them. It will react violently with water (hydrolyzes), DMSO, and ethanol. MNNG will also react with various nucleophiles, especially with amines and thiols. MNNG decomposes at 118-123.5 °C. MNNG is rapidly destroyed by 10% thiosulfate solution. Contact of MNNG with alkali produces the very toxic gas diazomethane. When heated to decomposition, it emits very toxic fumes of NO_x. MNNG will explode under high impact. MNNG is sensitive to heat, light and moisture (Sax and Lewis, 1987; Radian, 1991).

USE

MNNG currently has no known commercial use (IARC V.4, 1974). It is a research chemical used as an experimental mutagen, teratogen, and carcinogen (Sax and Lewis, 1987; Merck, 1989). Formerly, MNNG was used commercially to prepare diazomethane (IARC V.4, 1974; Merck, 1989).

PRODUCTION

N-Nitroso compounds are produced primarily as research chemicals and not for commercial purposes (USEPA, 1980). MNNG is not produced commercially in the United States. Import and export data have not been reported (HSDB, 1989; USITC, 1986, 1987, 1988, 1989).

EXPOSURE

No permissible occupational exposure limits have been established by OSHA, NIOSH, or ACGIH. The extent of exposure of the general population to MNNG is unknown, but exposure to nitrosamines in general is probably limited to industrial areas (USEPA, 1980). Occupational exposure may occur through inhalation of dust particles and dermal contact at workplaces where MNNG is used as a research chemical (IARC V.4, 1974; HSDB, 1998). The total worker exposure estimated for the National Occupational Exposure Survey (1981-1983) is 522 workers (NIOSH, 1984). Potential exposure of workers to MNNG may be limited to laboratory research and housekeeping personnel and those handling laboratory wastes including compound containers and inner linings; formulated feed mixes; bedding; animal carcasses; and any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill into water or on dry land. MNNG exists solely in particulate phase in the ambient atmosphere. It is not expected to volatilize from moist or dry soil surfaces. Hydrolysis is an important process in wet soils, with a half-life of 27 hours at a pH of 7 at 25°C (HSDB, 1998). MNNG is not expected to adsorb to suspended solids and sediments.

REGULATIONS

In 1980 CPSC preliminarily determined that *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine was not present in consumer products under its jurisdiction. Subsequently, public comment was solicited to verify the accuracy of this information; no comments were received. Pending receipt of new information, CPSC plans no action on this chemical. EPA regulates *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), and Resource Conservation and Recovery Act (RCRA). MNNG is a toxic pollutant of water. EPA has established effluent guidelines, rules for regulating hazardous spills, general threshold amounts, and requirements for handling and disposal of MNNG wastes. A reportable quantity (RQ) of 10 lb has been established for MNNG under CERCLA. OSHA regulates MNNG under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-84.